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SUBCONTRACTING PROGRESS REPORT
SF-294
10/1/96 - 3/31/97
01/01/96 - 3/31/97
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CORTICAL CONTROL OF NEUROPROSTHESES
Contract No: NO1-NS-6-2352

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This progress report contains: 1- text and figures describing our recent results on neuroprosthetic (NP) control of an external motion system in rats using real-time neurophysiological recordings in the forelimb area of the motor cortex, 2- descriptions of results using rats with recordings in the mouth area of the motor cortex, 3- plans for future studies, and 4- copies of abstracts submitted for talks at the upcoming Society for Neuroscience Meeting, relating to this work.

1- Neuroprosthetic Control from Forelimb Motor Cortex.

As briefly outlined in the previous progress report, we have implemented the plan outlined in the original RFP proposal to verify feasibility of NP control of an electromechanical arm in one dimension. In this, the rat first learns to move a manipulandum which proportionally controls movement of a "robot" arm (RA) from a source of water to the animal's mouth. The rat normally rewards itself by first pressing down the manipulandum, which moves the RA in position to get the water, and then releasing the bar, which moves the RA through a hole in a Plexiglas barrier to a position where the rat can drink it. We have now produced two rats in which up to 32 neurons were recorded simultaneously from the forelimb areas of the primary motor (MI) cortex and ventrolateral (VL) thalamus during the learning and performance of this task. In Rat1 we were subsequently able to train the rat to move the RA and reward itself using the weight-integrated activity of 32 neurons. The weights used for integrating this activity were derived from a principal components analysis (PCA) of the activity of the 32 most task dependent neurons. In Rat1, the first principal component (PC1) was observed to be most task dependent component, and therefore was used to set the weights. In Rat4, on the other hand, PC1 mainly expresses information from the numerous other neurons which are not correlated with forelimb movement. Therefore, we are using weightings from PC2, which more cleanly matches the forelimb movement. This is a nice test of the ability of different weighting schemes to optimize information extraction from the neuronal ensemble. Using this scheme, we are now close to repeating in Rat4 the successful NP controlled movement of the RA which was demonstrated in Rat1.

The included figures show the results from Rat1:

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Fig. 1: Spike waveforms of the 48 neurons simultaneously recorded from the forelimb areas of the MI cortex and VL of this animal during performance of the manipulandum movement task. Such waveforms are captured periodically during the recordings to assure their stability and stationarity over experimental time. Each cell shows a raster of several waveforms from the indicated single unit, captured over the same 30s period. The total time covered for each waveform is 2ms, with a pre-trigger time of 0.5ms. Amplitudes range from 100-500uV, and also vary here as a function of the indicated gain.

Fig. 2: Peri-event histograms showing the activity of 32 of these neurons averaged over the onsets of 29 manipulandum presses. The cell at top left ("nr_33") shows the measured position of the manipulandum, averaged over these trials. Units are arbitrary. Population vectors derived from the three principal components ("pca.pc1", etc.) are shown at the bottom right. Though some individual cells appear to encode the movement well, the PC population vectors provide much better statistical resolution on a trial-by-trial basis. All histograms cover the same 5s periods, with 2s pre-event.

Fig. 3: Average activities around manipulandum press ("barpress") of the population vectors derived from PCs 1 and 2, and the raw average. These show the selectivity of PC1 in its encoding of the forelimb manipulandum movement. Some task dependency is also seen for PC2 and the raw average, but with much less signal/noise.

Fig. 4: Stripcharts of PC1, PC2 and the Raw Average over the first 50s of the same experiment. The animal depressed the manipulandum, and received a water reward, seven times over this period. The stripcharts show that, on a trial-by-trial basis, PC1 produces the best statistical resolution of the manipulandum press.

Fig. 5: Stripcharts of the same PC1, PC2 and Raw Average over the first 50s of the following experiment in which the control of the RA was switched to the NP, which was controlled by the population vector PC1, whose weights were encoded in hardware by setting the values of 32 variable resistors. Over this time the animal successfully moved the RA to the water loading position("Load drop") four times, as indicated by the asterisks over PC1. These were all accompanied by forelimb actuated movements of the manipulandum, though in this case the animal quickly learned that only the initial phasic imposition of force on the manipulandum was necessary. This animal also made a few less forceful attempts which failed to reach the Load Drop position.

Fig. 6: Peri-event histograms of the 32 neurons averaged around the onset of 10 such NP induced RA movements. Though some neurons are shown by these averages to encode this movement well, on a trial-by-trial basis their individual contribution to the signal is far to variable to be of use in driving the RA.

2- Neuroprosthetic Control from the MI Mouth Area.

Rat2 and Rat3 received implants in the MI mouth area in order to test the rats' ability to learn to dissociate the neural activity in these areas from the overt movement with which they normally associated. These animals were initially trained, like the

others, to control the RA through movement of the manipulandum. Next, however, control was switched to the NP, which was driven by unweighted integration of MI neurons whose main activity was related to mouth movement. Thus, when the animal attempted to drink water from the RA, it moved rapidly back and forth in time with the rhythmic movements of the tongue and mouthparts. In order to drink, therefore, the animal had to somehow suppress this MI cortical activity, while still moving it's mouth sufficiently to get the water. We observed that over a period of several days, Rat2 and Rat3 learned to prevent this rhythmic movement of the RA and thus, to drink. We have not yet resolved, however, whether this might have been achieved purely by a change in the mouth movements, as opposed to an actual dissociation of MI cortical activity from movement. We intend to address this question in future animals by simultaneously recording EMG activity of masticatory muscles, or from their motor neurons in the motor nucleus of V.

3- Plans for the Future.

A. Rat Recordings.

i. Further resolve the issues discussed above through further recordings in more rats.

ii. Further attack the MI-movement dissociation problem by removing sensory and motor connections with the forelimb, either reversibly, by injecting lidocaine into the brachial plexus, or permanently, by amputating the forelimb.

B. Monkey Recordings.

i. We are now preparing to try these same types of experiments in the monkey, in Dr. Nicolelis' lab at Duke University. He has now shown splendid success in recording long term spiking activity from the MI and SI cortices in three monkeys. The next step is to build a setup in his lab like that in mine.

ii. Develop a two- or three-dimensional RA control setup, using 3D arm movement sensors recently obtained for the monkeys, and a 2- or 3D robot arm setup.

C. All Projects.

i. Explore other statistical and mathematical techniques to optimize control of the RA from brain cell activity.

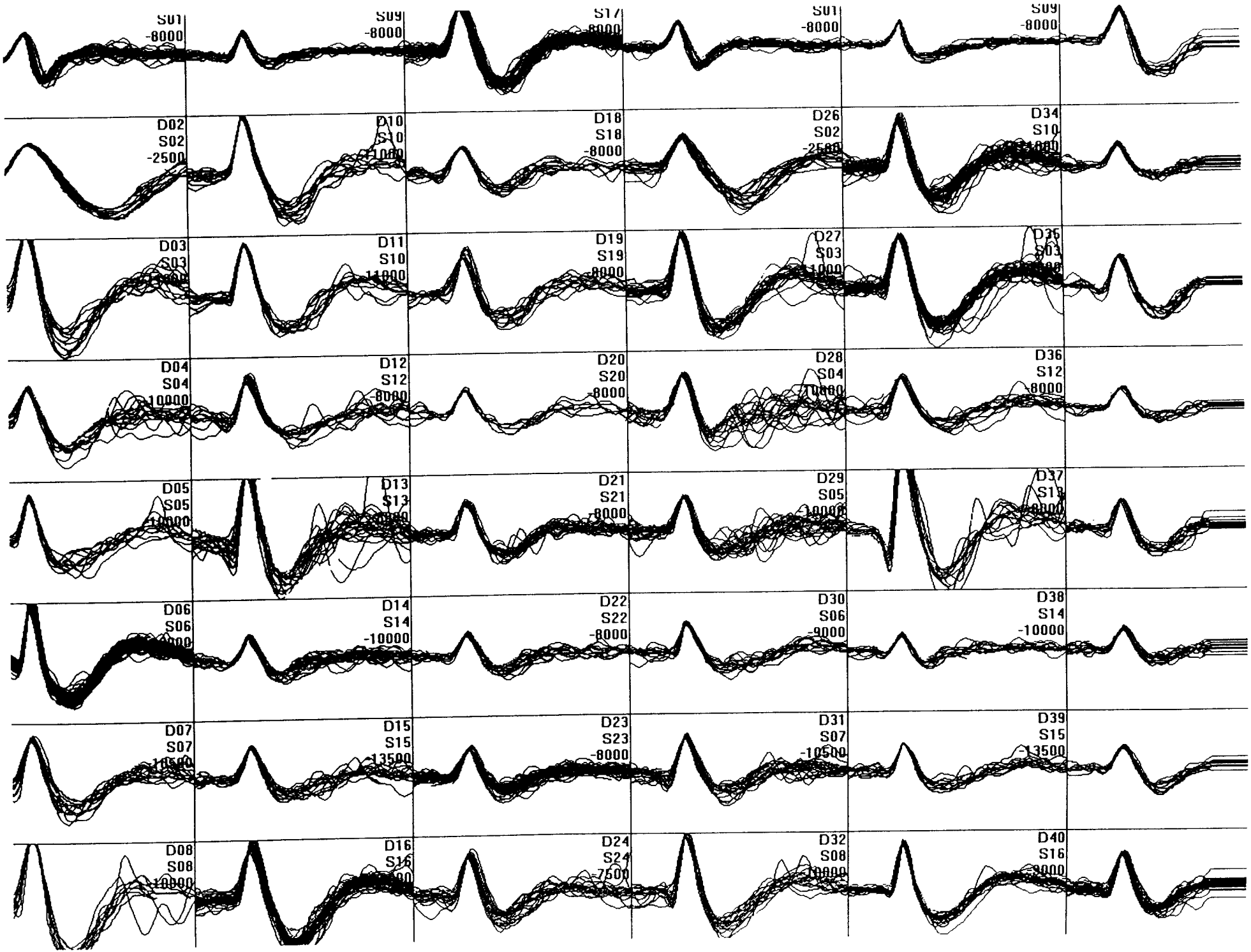
ii. Achieve, through collaboration with Spectrum Scientific (now Plexon Inc.), a general computer mediated real-time interface for motion control.

iii. Develop, in collaboration with other researchers in the Neuroprosthesis program, a common data base for sharing recorded data.

4. Abstract recently submitted for presentation at the Society for Neuroscience Meeting, 1997:

NEURAL POPULATION ACTIVITY IN SENSORIMOTOR CORTEX CAN CONTROL AN EXTERNAL "ARM" MOVEMENT SYSTEM. J.K. Chapin[*1], R.S. Markowitz[1], K.A. Moxon[1] and M.A.L. Nicolelis[2], [1]Dept. Neurobiol., Allegheny U. Hlth. Sci., Phila, PA; [2]Dept. Neurosci., Duke U., Durham, NC.

To assess the importance of population coding in the primary motor (MI) cortex, neuronal ensembles were simultaneously recorded through chronically implanted arrays of electrodes in the forelimb areas of the MI cortex and the ventrolateral (VL) thalamus of rats trained to obtain a water reward by moving a manipulandum which was configured to proportionally move a mechanical arm (MA) from a water source to the rat's mouth. The simultaneous activities of 32 simultaneous single units were recorded in the MI and VL during performance of this task. Next, the data from these neurons were subject to a principal components analysis (PCA) to extract an eigenvector weighting matrix which weighted these neurons according to their task related activity. These weights were then implemented on 32 channel spike integration circuit whose output could be used to control the MA. By switching the control of the MA from the manipulandum to the neural population (NP), the rat was able to obtain its water reward through direct real-time translation of ongoing MI and VL neural ensemble activity. When under this NP control, the MA movement accurately followed the phasic activity of these neurons around the onset of manipulandum movement, but were not maintained during the position holding phase. Nonetheless, the rats NP were able to move the MA and obtain the water reward with a nearly 100% reliability. Over 90% of the recorded neurons were found to contribute to the smooth control of the MA, its precision increasing as a function of the number of neurons used. The precision increased still further when clusters of 2-4 units were used rather than single units. These results suggest that large neural populations in the MI and VL can precisely encode the onset phase of forelimb movement. *Supported by NIH N01-NS-6-2352, NIH RO1-NS26722, and ONR N00014-95-1024 to JKC.*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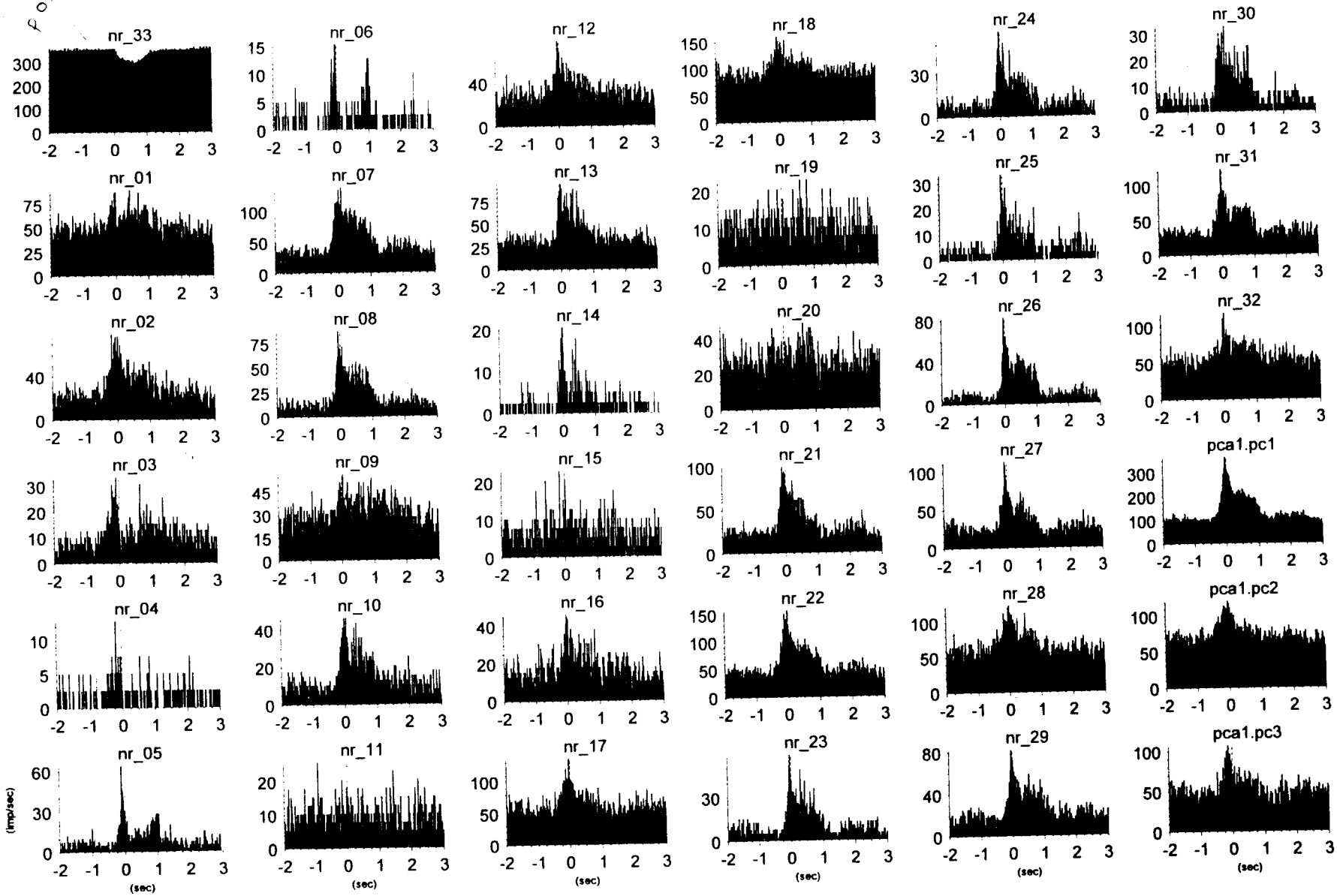
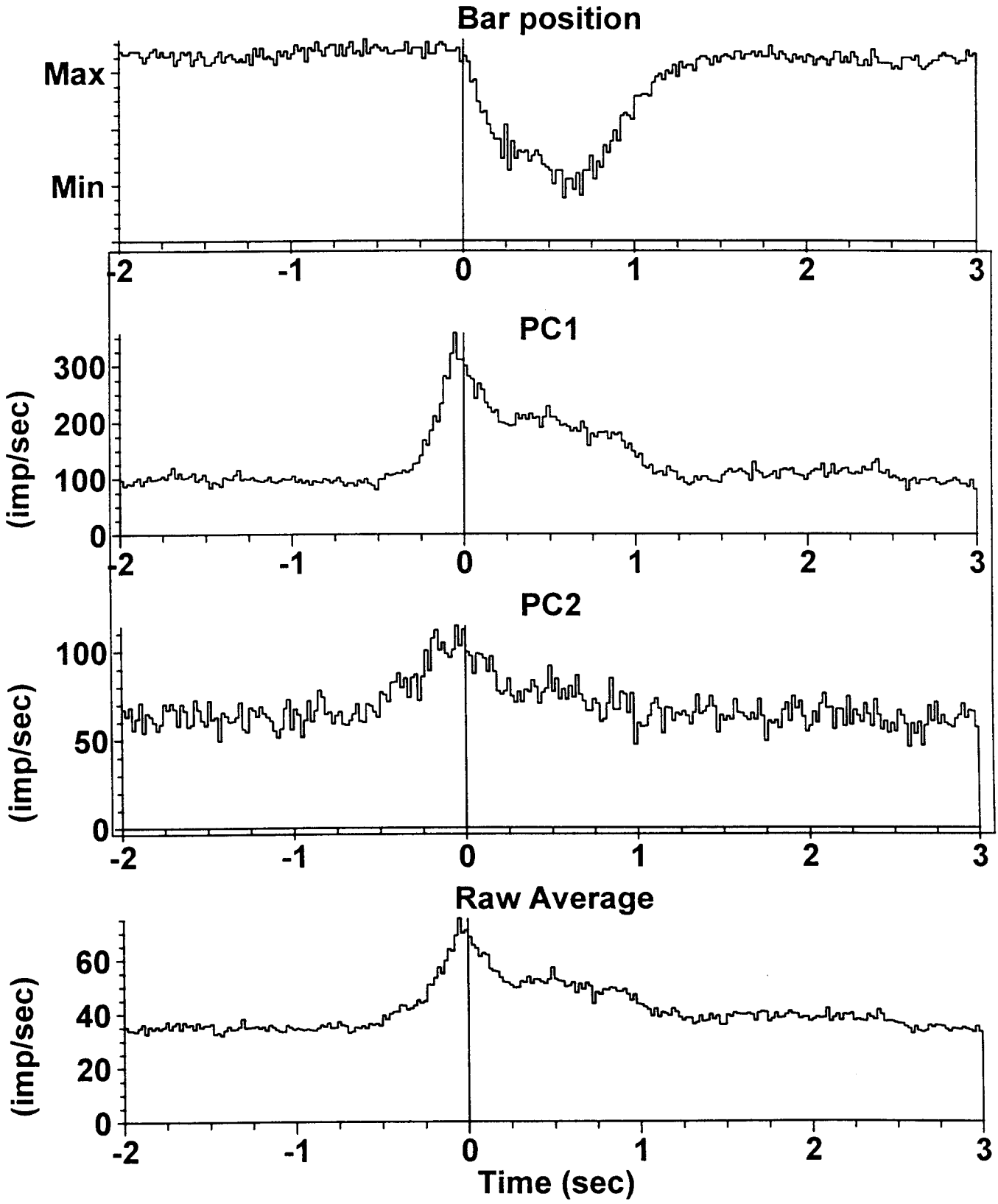
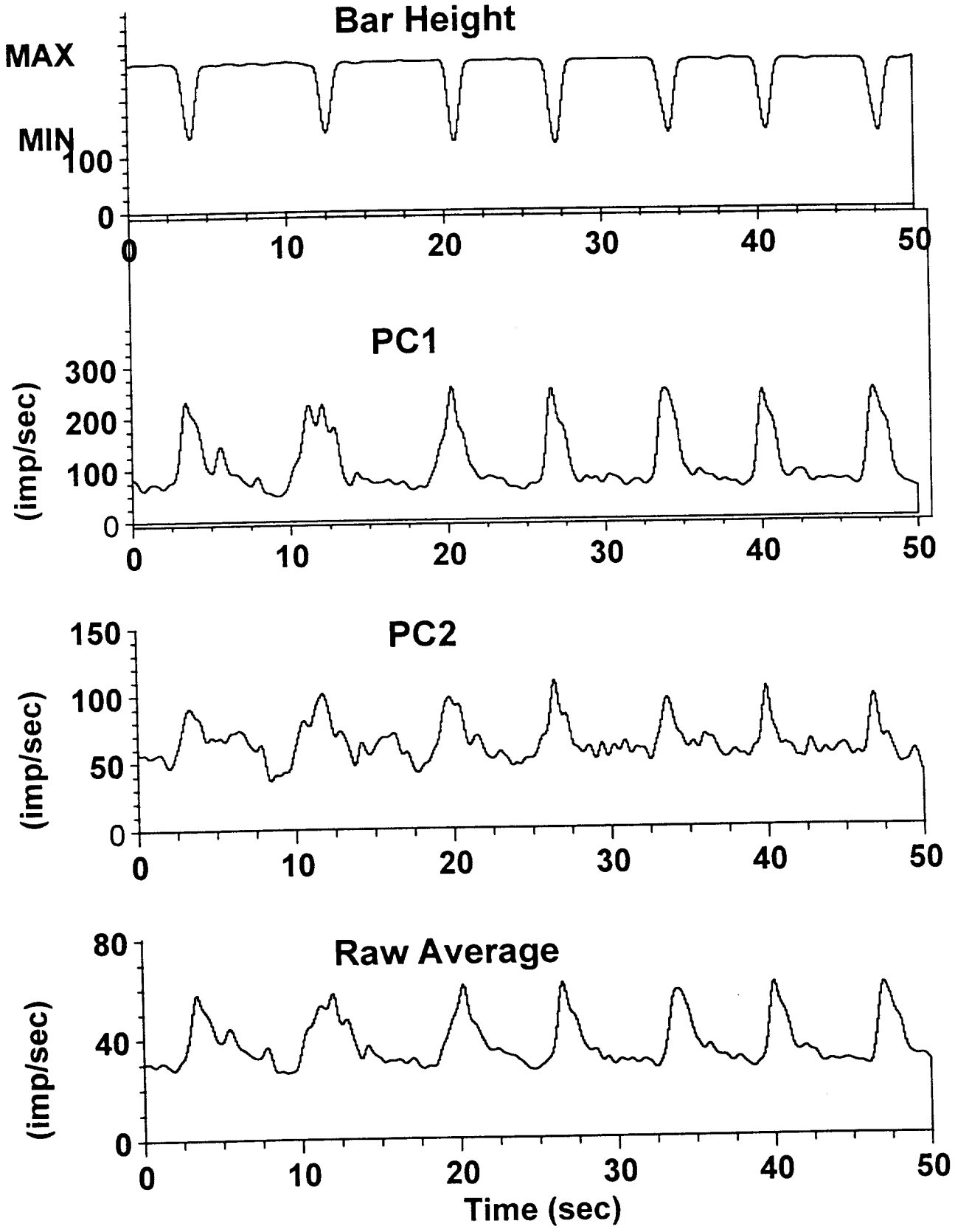
AVERAGE NEURONAL RESPONSES TO BARPRESS



AVERAGE RESPONSE OF POPULATION VECTORS AROUND BARPRESS



CORRELATION OF POPULATION VECTORS WITH BAR PRESS



MOVEMENT OF ROBOT ARM WITH POPULATION VECTOR ACTIVITY